

In re Application of:

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PATENT

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AMENDMENTS TO THE SPECIFICATION

Please amend paragraph [0168] of the specification as follows:

[0168] It was next determined whether a method of the present invention can be performed using DNA rather than RNA. SEQ ID NO:1 provides a differentially methylated region (DMR) within IGF2 that shows hypomethylation in CRC with LOI (Cui H. et al., *Cancer Res.* 62, 6442-6446 (2002), incorporated herein in its entirety by reference). In order to determine whether a hypomethylation defect occurs in PBL and colon of patients without known neoplasia, we examined 24 samples, 12 from normal tissues (6 PBL, 6 matched normal colonic mucosa) with normal imprinting, and 12 from normal tissues (6 PBL, 6 matched normal colonic mucosa) with LOI. In all 12 tissues with normal imprinting, IGF2 showed a normal pattern of half-methylation (Fig. [[1A]]2A). In contrast, in 11 of 12 samples from normal tissue with LOI, IGF2 showed hypomethylation of the IGF2 DMR; in the other sample, IGF2 showed partial methylation of both alleles but was nevertheless abnormal (Fig. [[1B]]2B). The significance of hypomethylation between normal tissues with and without LOI was $p < 0.0001$ (Fisher's exact test). In contrast, H19 showed hypomethylation in all cases, regardless of imprinting status (data not shown). Thus, aberrant IGF2 methylation is linked to LOI in normal colon and lymphocytes, just as it is in CRC.